UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/081,885	02/20/2002	Stephen J. Kaufman	94-00	9945

23713 7590 07/01/2003

GREENLEE WINNER AND SULLIVAN P C
5370 MANHATTAN CIRCLE
SUITE 201
BOULDER, CO 80303

EXAMINER
HADDAD, MAHER M

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 07/01/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)
10/081,885	KAUFMAN, STEPHEN J.
Examiner	**Art Unit**
Maher M. Haddad	1644

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 April 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *4-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8*
4)☐ Interview Summary (PTO-413) Paper No(s) _____
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

1. Claims 1-23 are pending.

2. Applicant's election with traverse of Group I, claims 1-3 drawn to a method of identifying an individual exhibiting symptoms of muscular dystrophy as an individual suffering from scapuloperoneal muscular dystrophy comprising obtaining a tissue and determine the level of the translation of the $\alpha 7\beta 1$ integrin using an antibody in filed on 4 22 03, is acknowledged.

Applicant's traversal is on the grounds that Group I, wherein the method utilizes antibody and Group II, wherein the method utilizes primers would identify the same type of muscular dystrophy and measures expression of the same gene, $\alpha 7\beta 1$ integrin. Further, claim 1 is a linking claim which links the Group I and Group II claims and because of the common technical feature of measuring integrin expression, claims 1-6 should be examined and a search of both Groups would not constitute an undue burden on the patent office. This is not found persuasive because the specific antibodies and primers are recognized divergent subject matter. In addition, the antibodies and primers are distinct because their structures are different. Therefore the methods of identifying an individual exhibiting symptoms of muscular dystrophy as an individual suffering from scapuloperoneal muscular dystrophy comprising obtaining a tissue using an antibody primers are distinct and independent, and searches of all groups would place an undue burden upon the examiner due to the distinct and divergent subject matter of each Group.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 4-23 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

4. Claims 1-3 are under examination as they read on a method of identifying an individual exhibiting symptoms of muscular dystrophy as an individual suffering from scapuloperoneal muscular dystrophy comprising obtaining a tissue and determine the level of the translation of the $\alpha 7\beta 1$ integrin using an antibody.

5. Claim 3 is objected to because of the following informalities: the phrase "integrin-specificantibody" is misspelled. Appropriate correction is required.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention

7. Claims 1-3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claim 1 is indefinite for being incomplete for omitting essential elements, such omission amounting to a gap for the detection step. The omitted element is: the antibody that specifically binds $\alpha 7\beta 1$ integrin to detect the translation product.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for identifying an individual exhibiting symptoms of a muscular dystrophy wherein the said individual suffering from scapuloperoneal muscular dystrophy comprising (a) obtaining a muscle tissue sample from an individual exhibiting symptoms of a dystrophy, wherein said muscle tissue sample is obtained from a tissue known in a normal individual to express $\alpha 7\beta 1$ integrin, (b) detecting the $\alpha 7\beta 1$ integrin by contacting the muscle tissue sample using an $\alpha 7\beta 1$ integrin-specific antibody in the said sample, (c) determining a level of the transcription the $\alpha 7\beta 1$ integrin in said muscle tissue sample as compared with a level of the $\alpha 7\beta 1$ integrin in said muscle tissue sample which is lower than the level in a muscle tissue sample from the same muscle tissue of a normal individual, does not reasonably provide **enablement** for a method fro identifying an individual exhibiting symptoms of a muscular dystrophy as an individual suffering from scapuloperoneal muscular dystrophy, said method comprising the steps of: (a) obtaining any tissue sample from an individual exhibiting symptoms, wherein said tissue sample is obtained from a tissue known in a normal individual to express $\alpha 7\beta 1$ integrin, (b) detecting a translation product of an $\alpha 7\beta 1$ integrin gene in said tissue sample, (c) determining a level of the translation product of the $\alpha 7\beta 1$ integrin gene in said tissue sample as compared with a level of the transcription or translation product of the $\alpha 7\beta 1$ integrin gene in any tissue sample from the same tissue of a normal individual, whereby scapuloperoneal muscular dystrophy is diagnosed when the tissue sample of an individual exhibiting muscular dystrophy symptoms comprises a level of a transcription or translation product of the $\alpha 7\beta 1$ integrin gene in any tissue sample from the same tissue of a normal individual in claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with this claim.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

Besides muscle tissue sample, the specification fails to provide any guidance as to how to use any tissue sample to identify scapuloperoneal muscular dystrophy. Further, beside the antibody against $\alpha 7\beta 1$ and $\alpha 7$ the specification fails to provide sufficient guidance regarding the translation product detection step.

Therefore, there is insufficient direction or objective evidence as to how to use any tissue sample or any translation detection technique in a method for identifying an individual exhibiting symptoms of scapuloperoneal muscular dystrophy as to whether such a desired determination can be achieved or predicted, as encompassed by the claims.

In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification, and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Hayashi *et al* (Nature Genetics 19:53-64, May 1998, IDS ref. = C29) as is evidenced by the specification on page 22, lines 7-13.

Hayashi *et al* teach a method for identifying an individual exhibiting symptoms of a muscular dystrophy. The method comprising obtaining 6,500 diagnostic muscle biopsies from 117 patients who carried the clinical diagnosis of "unclassified" congenital myopathy and congenital muscular dystrophy using immunocytochemistry analysis with antibodies against the extracellular domain of integrin $\alpha 7$, integrin $\beta 1D$, $\alpha 2$ laminin, and dystrophin, wherein the antibodies were detected using a secondary antibodies such as FITC-labelled goat $F(ab')^2$ anti-mouse and anti-rabbit IgG . Hayashi *et al* further determined the level of $\alpha 7$ integrin expression by comparing the level of $\alpha 7$ translation product gene in the skeletal muscle samples from control and three patients with primary integrin $\alpha 7$ deficeney. Finally, Hayashi et al teach that the three patients exhibited integrin $\alpha 7$ deficiency but show normal expression laminin $\alpha 2$ chain.

β-dystroglycan and α-sarcoglycan (see the entire document and page 53, col., 2, figure 1 and methods on pages 96-97 in particular).

While Hayashi *et al* reference teachings may be silent as to the "individual suffering from scapuloperoneal MD", the patients identified by Hayashi *et al* had the same characteristics as the scapuloperoneal MD, specially because all three patients had normal levels of laminin (merosin). Further as is evidenced by the specification on page 22, lines 7-13, that all SPMD patients analyzed have laminin-2 4 in the matrix surrounding muscle fibers, indication that the reduction or lack of α7 integrin is not secondary to the loss of laminin-2 4 (merosin).

Further, while Hayashi *et al* used anti-α7 antibodies to detect α7β1, the anti-α7 antibodies would inherently detect the levels of α7β1 integrin complex, because α7 integrin subunit forms a complex with β1. Thus detecting α7 subunit of the complex would detect the α7β1 integrin complex as a whole.

Since the office does not have a laboratory to test the reference anti-α7 antibodies would detect α7β1 integrin and the reference patients suffering from scapuloperoneal MD, it is applicant's burden to show that the reference antibody does not bind to the α7β1 integrin and the reference patients are not suffering from scapuloperoneal MD recited in the claim. See In re Best, 195 USPQ 430, 433 (CCPA 1977); In re Marosi, 218 USPQ 289, 292-293 (Fed. Cir. 1983); and In re Fitzgerald et al., 205 USPQ 594 (CCPA 1980).

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

12. Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hayashi *et al* (Nature Genetics 19:53-64, May 1998, IDS ref. # C29) as is evidenced by the specification on page 22, lines 7-13 in view of Hodges et al (Journal of Cell Science 110:2873-2881, IDS Ref. # C31).

The teachings of Hayashi *et al* reference have been discussed, supra.

The claimed invention differs from the reference teachings only by the recitation of α7β1 integrin-specific antibody in claim 2 wherein the α7β1 integrin-specific antibody is detectably labeled in claim 3.

Hoges et al teach that the antiserum 347 reacts in immunofluorescence and western blot analyses with native and denatured α7β1 integrin and binding is inhibited by prior reaction with 100 μg ml of the immunizing peptide (page 2874, 2nd col., 2nd ¶ in particular). Further, Hodges et al teach that the α7β1 integrin is the primary laminin receptor on skeletal myoblasts and adult

myofibers. Hodges *et al* also teach that immunofluorescent demonstrates an increases in $\alpha 7\beta 1$ integrin in patients with Duchenne MD and in mdx mice that lack dystrophin. While the levels of $\alpha 7\beta 1$ integrin are severly diminished in patients with laminin $\alpha 2$ chain congenital dystrophy muscular dystrophy and in *dy dy* mice that also do not make the $\alpha 2$ laminin chain (see abstract on page 2873 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the anti-$\alpha 7$ antibodies taught by Hayashi et al with the antiserum 347 antibodies that that reacts with native and denatured $\alpha 7\beta 1$ integrin in a method for identifying an individual exhibiting symptoms of a muscular dystrophy as an individual suffering from SPMD.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so because the $\alpha 7\beta 1$ integrin is the primary laminin receptor on skeletal myoblasts and adult myofibers as taught by Hodges *et al*.

From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
June 30, 2003

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600